Annotations

Exercise-induced asthma

It has been known for nearly 300 years that exercise can provoke an attack of breathlessness¹ and every paediatrician has heard asthmatic children complain that exercise makes them ill, so much so that they are often prohibited from taking part in physical activity. The typical attack of exercise-induced asthma (EIA) is provoked by 4 to 6 minutes of moderately severe to severe continuous exercise—such as running 1000 metres. During the exercise the child feels well as there is some bronchodilatation which gives way to bronchospasm towards the end of the run, and the really pronounced fall in lung function only occurs some 3 to 5 minutes after stopping the exercise.² Thus EIA is really post-exercise asthma, and it is unusual for the attack to develop so rapidly that the child has to stop in the middle of exercise. Not all exercise has the same potential for causing asthma even if equally severe. Some studies have shown that swimming rarely causes EIA³ and likewise intermittent exercise—such as in most team sports—is less asthmagenic than continuous exercise.⁴ The reasons for these differences are becoming clearer as will be seen but they have practical importance; thus many well known athletes have excelled in swimming despite being active asthmatics.⁵ Young children with asthma often cough when they have bronchospasm, and so characteristic of asthma is the attack provoked by exercise that any child with post-exercise cough, breathlessness, or wheeze should be considered asthmatic unless proved otherwise.

Pathophysiology

Because it serves as a model of asthma in general, much interest has been taken in the pathways by which EIA is provoked. The similarity of the brief attack to acute antigen-induced asthma and its response to drugs—such as salbutamol and sodium cromoglycate—led to the concept that EIA was due to the release of chemical mediators of bronchospasm from stores in mast cells. Of particular importance was the observation that sodium cromoglycate inhibited EIA only if given before exercise but not if given after it but before the development of the attack.⁶ In addition it was shown that once an attack of EIA had occurred the patient remained

fairly unresponsive (refractory) to a second attack for a period of time with a half-life of about one hour.⁷ Recently there have been some direct observations in support of this model from the work, among others, of Lee *et al.*⁸ who showed that neutrophil chemotactic factor, a mast cell-derived mediator, was released during the exercise which preceded EIA. Both the release and the EIA were inhibited by pretreatment with sodium cromoglycate.

An alternative hypothesis was developed as a result of the observations by a number of investigators that EIA was attenuated and even abolished if the patient breathed warm humid air. In a powerful series of studies the group headed by McFadden showed this to be due to the prevention of cooling of the airways which occurs during hyperventilation or exercise, and they were led to conclude that EIA was simply a manifestation of hyperventilation-induced asthma.⁹ They postulated that the hyperventilation cooled the airways and evoked bronchospasm through some neural reflex. Since they found no mediator release in hyperventilation-induced asthma, they believed that mediators were not involved in EIA, while the different asthmagenicity of various types of exercise was explained by differing amounts of airways cooling—that is during swimming the air breathed was humid and less heat was lost in the humidification of inspired air by the lungs. Some recent experiments have cast serious doubt on this hypothesis. Thus (a) there still remains a difference, albeit a small one, between running and swimming when the respiratory heat loss is matched, (b) the fall in lung function lags behind the airway cooling by several minutes and remains low when airway temperature has returned to baseline, and (c) it is possible to induce a refractory period by exercise breathing warm humid air which does not itself provoke EIA.¹⁰

At the present time it seems likely that EIA does involve mediator release and that it is not simply owing to hyperventilation, although the temperature changes in the large central airways undoubtedly influence the response to exercise. To complicate matters still further there is some evidence to suggest that the refractory period after EIA may be due to lack of response of the target smooth muscle cell rather than to mediator depletion.

Management

Management of EIA depends on eliciting a history of post-exercise wheeze or cough, supplemented if necessary by laboratory confirmation. Perhaps the most essential part of management is to explain to the parents the nature of the problem, to stress that adequate treatment is available, and that under no circumstances should the child be prevented from participating in normal activity although he may need to be helped by appropriate medication.

Studies have shown that a number of drugs can inhibit EIA if given before exercise.¹¹ Without a doubt the most effective is an inhaled beta-2 sympathomimetic agent such as 2 puffs of salbutamol or terbutaline taken between 5 and 10 minutes before exercise. Interestingly oral sympathomimetic agents are believed by some to be ineffective in preventing EIA. The protective effects of sodium cromoglycate and theophylline are less than the sympathomimetics. Sodium cromoglycate is also effective immediately after its inhalation in the majority of children but most of the effect wears off after about 2–3 hours. The effect of theophylline is dose dependent and it is not a suitable drug to use to prevent EIA on a p.r.n. basis. Most studies have failed to show any benefit from steroids in the majority of children with EIA, while the value of atropine derivatives remains controversial. EIA is chiefly a problem of older children who can generally be taught to use a pressure-packed aerosol sympathomimetic and they should be instructed to use it before any exercise which, from experience, they know is likely to cause trouble. For the young child one can only recommend wet-nebulised sympathomimetics or sodium cromoglycate but this is

obviously very inconvenient. Any child on regular maintenance treatment with sodium cromoglycate, theophylline, or aerosol steroids may still need to take an additional aerosol sympathomimetic if EIA remains troublesome.

References

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Footnote

British paediatricians can well be proud that one of their number, Dr R S Jones, and his colleagues are largely responsible for the modern interest in EIA and predicted much of what we now know from their simple, clinical, and physiological observations in children.¹²

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